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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,630	06/27/2003	Zcina Tannous	MGH-036AUS	8743

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DALY, CROWLEY, MOFFORD & DURKEE, LLP  
SUITE 301A  
354A TURNPIKE STREET  
CANTON, MA 02021-2714

EXAMINER

SANG, HONG

ART UNIT PAPER NUMBER

1643

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/607,630	TANNOUS ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

**RE: Tannous et al.**

Applicants called examiner on 3/14/2006 and pointed out an error that was inadvertently made by the examiner in the office action mailed on 2/7/2006. The previous office action is therefore vacated and the new office action is set forth below.

1. The information disclosure statement (IDS) filed on 6/27/2003 has been considered. A signed copy is attached hereto.
2. Claims 1-11 are currently pending and under examination.

### ***Specification***

3. The disclosure is objected to because of the following informality. The Brief Description of the Drawings does not reference each of the Figures. The Brief Description should be amended to reference Figures 5A and 5B. Correction is required.

### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Richards-Kortum et al. (US Patent No. 6,187,289 B1, Date of Patent 2/13/2001, effective filing date 10/20/1998).

Claims 1 and 10 is drawn to a method of enhancing optical characteristics of at least one cell anomaly associated with a tumor, comprising: (a) applying a predetermined contrasting solution to an *in-vivo* defect area associated with the tumor for optically enhancing the at least one cell anomaly associated with the tumor; and (b) imaging at least a portion of the *in-vivo* defect area associated with the tumor using a first optical imaging system to provide an *in-vivo* enhanced tumor image, wherein the *in-vivo* enhanced tumor image includes the at least one cell anomaly having enhanced attributes. The method is further limited wherein imaging using the first optical imaging system includes imaging using a confocal microscope.

Richards-Kortum et al. teach a method of using acetic acid as a contrast agent for confocal imaging of cells *in vivo* comprising the steps of (a) applying acetic acid to a diagnostic tissue sample in sufficient concentration to induce an alteration of the index of refraction of nuclei in the cells; and (b) imaging the cells using a reflectance confocal imaging system (see claims 1 and 4). Richards-Kortum et al. teach that after the addition of acetic acid, images of tissue can be obtained which illustrate characteristic differences between normal and neoplastic tissue throughout the entire epithelial thickness (see column 4, lines 31-41).

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richards-Kortum et al. (US Patent No. 6,187,289 B1, Date of Patent 2/13/2001, effective filing date 10/20/1998) in view of Yamamoto (US Patent No. 4,395,398), Prevendar (US Patent No. 6,652,840, effective filing date at least 2/8/2002) and Klaveness et al. (US Patent No. 6,159,445) and Rajadhyaksha et al. (J. Invest. Dermatol. 1999, 113: 293-303).

The interpretations of claims 1 and 10 are set forth above (see paragraph 5).

Claims 2-9 and 11 embody claim 1, wherein applying the predetermined contrasting solution to the in-vivo defect area includes applying an AlCl solution having a predetermined concentration of Al and a predetermined concentration of Cl, applying the AlCl solution includes applying an AlCl solution having a concentration ranging from approximately 20% to approximately 40%, and applying the predetermined contrasting solution to the in-vivo defect area includes applying a solution of AlCl (hexahydrate) 20% w/v in anhydrous ethyl alcohol (S.D. alcohol 40) 93% v/v, the method further including step (c) freezing an excised predetermined layer of the in-vivo defect area associated with the tumor, step (d) imaging the excised predetermined layer of the in-vivo defect area associated with the tumor using a second predetermined optical

imaging system to provide an ex-vivo enhanced tumor image, step (e) comparing the in-vivo enhanced tumor image and the ex-vivo tumor image to investigate the presence of the at least one cell anomaly, the method further includes: after step (a) applying sterile water to the in-vivo defect area for further optically enhancing the at least one cell anomaly, after step (a) applying an optically transparent sterile tape to the in-vivo defect area for sterilizing the in-vivo defect area, imaging using the second predetermined optical imaging system includes imaging using a microscope.

The teachings of Richards-Kortum et al. are set forth above as they apply to claims 1 and 10 (see paragraph 5 above).

Richards-Kortum et al. do not teach using 20-40% AlCl solution. Richards-Kortum et al. do not teach using a solution of AlCl 20% in anhydrous ethyl alcohol. Richards-Kortum et al. do not teach using sterile water and optically transparent sterile tape. Richards-Kortum et al. do not teach freezing and imaging an excised predetermined layer of the *in-vivo* defect area associated with tumor using a microscopy and comparing the *in vivo* tumor image with ex-vivo tumor image. However, these teachings are made up for in the teachings of Yamamoto, Prevendar, Klaveness and Rajadhyaksha.

Yamamoto teaches that an aqueous solution containing 10-40 w/v% of aluminum chloride can be used as a hemostatic composition for local application to small hemorrhages in the dental field, for example, bleeding from gums which occurs during dental surgery (see column 1, lines 8-16 and 67-68). Yamamoto teaches a hemostatic solution of 25% AlCl in 20% ethanol and 50% ethanol (see Examples 6 and 7).

Prevendar teaches that an aqueous solution of aluminum chloride can also be used to stop bleeding and seal open small blood vessels while accelerating the healing process of skin (epithelial) tissues (see column 2, lines 29-31).

Klaveness teaches the use of particulate materials as contrast agents in *in vivo* light imaging including confocal microscopy (see abstract and column 8, line 48). Tumor can be imaged using said method (see column 18, line 63). Klaveness teaches unlike all the light imaging dyes or contrast agents described in the state of the art that enhance contrast by changing the incident light absorption and/or fluorescence, the particulate materials enhance contrast by changing light scattering (see column 7, lines 49-65).

Rajadhyaksha et al. teach a method of *in vivo* imaging of human normal and abnormal skin using confocal scanning laser microscopy (see abstract, left column, lines 406) and comparison with histology (see page 299, left column, lower section) and confocal images of hematoxylin and eosin-stained skin (see page 300, left column). Rajadhyaksha et al. teach using water or cane-sugar solutions as immersion media to further enhance the contrast (see page 294, 2<sup>nd</sup> paragraph, lines 32-34, and 3<sup>rd</sup> paragraph, last sentence). Further Rajadhyaksha et al. teach using medical-grade adhesive tape to attach the ring and template to skin (see page 295, under skin-contact device).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include 20%-40% AlCl<sub>3</sub> solution, or a solution of 20% AlCl<sub>3</sub> in anhydrous alcohol in the method of Richards-Kortum et al. in view of the

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teachings of Yamamoto, Prevendar and Klaveness. One would have been motivated to include 20%-40% AlCl solution, or a solution of 20% AlCl in anhydrous alcohol in the method of Richards-Kortum et al. because AlCl solution provides two advantages as taught by Yamamoto, Prevendar and Klaveness. The first advantage of using AlCl solution is that aluminum solution can be used to stop bleeding during and/or after surgery. Because the method of Rajadhyaksha et al. involves excising a layer of tissue for ex-vivo imaging, one would be motivated to use AlCl solution to stop tissue bleeding caused by excising the tissue. The second advantage of using AlCl solution is that AlCl when prepared in anhydrous alcohol forms fine particles that can change light scattering and enhance the contrast of image. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to include 20%-40% AlCl solution, or a solution of 20% AlCl in anhydrous alcohol in the method of Richards-Kortum et al. because Richards-Kortum et al. teaches the method of *in vivo* tumor imaging using a contrasting solution, and AlCl solution has been used in clinical practice for stopping bleeding.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include sterile water and tape in the method of Richards-Kortum et al. and further comparing the *in vivo* image with ex-vivo image in view of the teachings of Rajadhyaksha. One would have been motivated to include sterile water and tape in the method of Richards-Kortum et al. and further comparing the *in vivo* image with ex-vivo image because Rajadhyaksha et al. teach that specific features are better delineated in the histology sections than *in vivo* and ex-vivo images



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provides additional insight into the interpretation of *in-vivo* confocal image (see page 300, 1<sup>st</sup> paragraph, lines 6-11), water can further enhance the image contrast and tape can be used to attach the ring and template to skin. While Rajadhyaksha et al. do not disclose the tape is for sterilizing the tissue, the medical grade tape used by Rajadhyaksha would inherently sterilize the tissues when it is applied to the skin. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to include sterile water and tape in the method of Richards-Kortum et al. and further comparing the *in vivo* image with *ex-vivo* image because Richards-Kortum et al. teaches the method of *in vivo* tumor imaging using a contrasting solution, Rajadhyaksha et al. teach a method of *in vivo* imaging using confocal microscopy and comparison of *in vivo* image with *ex-vivo* image.

### **Conclusion**

9. No claims are allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang  
Art Unit: 1643  
Mar. 16, 2006



LARRY R. HELMS, PH.D.  
SUPERVISORY PATENT EXAMINER